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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/457,926	12/08/1999	BURTON G. CHRISTENSEN	032367-449	8221
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27038 7590 12/18/2001

ADVANCED MEDICINE, INC.
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EXAMINER

GARCIA, MAURIE E

ART UNIT	PAPER NUMBER
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1627

DATE MAILED: 12/18/2001

22

Please find below and/or attached an Office communication concerning this application or proceeding.

File copy

Office Action Summary

Application No.
09/457,926

Applicant(s)
Christensen et al

Examiner
Maurie E. Garcia, Ph. D.

Art Unit
1627



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE THREE MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Oct 9, 2001

2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle* 35 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 41-46, 49-51, 53-55, 57, and 58 is/are pending in the application

4a) Of the above, claim(s) 42, 44-46, 57, and 58 is/are withdrawn from consideration

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 41, 43, 49-51, and 53-55 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirements

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

19) ☐ Notice of Informal Patent Application (PTO-152)

17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). 15

20) ☐ Other:

DETAILED ACTION

1. The Response filed October 9, 2001 (Paper No. 19) is acknowledged. Claims 41, 43, 49, 53 and 55 were amended, claims 47, 48, 52 and 56 were cancelled and claims 57 and 58 were added. Therefore, claims 41-46, 49-51, 53-55, 57 and 58 are pending.

Further consideration has necessitated new rejections. Since the new rejections were not entirely necessitated by amendment to the claims, the case is maintained in non-final status.

Election/Restriction

2. Claims 42 and 44-46 remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected species, there being no allowable generic claim. Applicant is reminded that **only** upon the allowance of a generic claim are they entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

3. Regarding newly added claims 57 and 58: Applicant made an election of species in Paper No. 10. At the time of the Restriction Requirement, the examiner noted that claims 43, 53 and 54 read on the elected species of formula (b). Thus, the election of species was treated as formula (b) with specific election of the species recited in claim

53. There were no other claims at this time that were drawn to other species of formula (b). Also, because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement with respect to the species election, the election was treated as an election without traverse (MPEP § 818.03(a)) (see previous Office Action).

4. Thus, claims 57 and 58 are withdrawn from consideration for two reasons:

- (1) Only upon the allowance of a generic claim are applicants entitled to consideration of claims to additional species (see paragraph 2 above); and
- (2) Newly submitted claims 57 and 58 are directed to a species that is independent or distinct from the species originally claimed (i.e. in claim 53). Since applicant has received an action on the merits for the originally presented species, this species has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 57 and 58 withdrawn from consideration as being directed to a non-elected species. See 37 CFR 1.142(b) and MPEP § 821.03.

5. However, after further consideration of applicant's arguments, amendments and the prior art, previously withdrawn claims 50 and 51 drawn to non-elected species are now examined on the merits.

6. Therefore, claims 41, 43, 49-51 and 53-55 are examined on the merits in this action.

Withdrawn Rejections/Objections

7. The objection to the Abstract is withdrawn in view of the amendments thereto. All of the previous rejections under 35 U.S.C. 112, first and second paragraphs are withdrawn in view of applicant's amendments to the claims. The provisional rejection under 35 U.S.C. 102(e) over application no. 09/317,198 is withdrawn in view of the abandonment of said application and the submission of a claim of priority to said application in the instant application. The rejection under 35 U.S.C. 102(f) is withdrawn in view of the clarification as to the inventor of this subject matter. Furthermore, all of the provisional double patenting rejections are withdrawn in view of the abandonment of the previously copending applications. Lastly, the previous rejection under 35 U.S.C. 103(a) is withdrawn in view of applicant's amendments and arguments.

Information Disclosure Statement

8. Applicants submission in the Response filed October 9, 2001 is sufficient for the concise explanation of the relevance for the non-English language document in the information disclosure statement filed September 13, 2000. Thus, previously unconsidered reference EP 322810 has been considered and a fully signed copy of the PTO-1449 is enclosed with this action. Additionally, the supplemental information disclosure statement filed September 7, 2001 has been considered and a signed copy of the PTO-1449 is also enclosed.

Inventorship

9. In view of the papers filed October 9, 2001, it has been found that this nonprovisional application, as filed, through error and without deceptive intent, improperly set forth the inventorship, and accordingly, this application has been corrected in compliance with 37 CFR 1.48(a). The inventorship of this application has been changed by addition of inventor John L. Pace.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

11. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not

commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 41, 43, 49-51 and 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Truett (US 5,693,791; on PTO-1449) in view of Boeckh et al (Antimicrob. Agents Chemother., 1988, Vol. 32, No. 1, pp. 92-95; of record) and Renoud-Grappin et al (Antiviral Chem. and Chemotherapy, Vol. 9, No.3, 1998, pp. 205-223) and Staroske et al (Tet. Lett., 1998, Vol. 39; on PTO-1449).

Truett teaches the "linking of diverse antibiotic moieties via difunctional organic compounds" (see column 1, lines 8-9). Specifically, dimers are taught having the structure A-L-B, where A and B are various antibiotic moieties (see "Summary", columns 1-6, especially column 1, lines 46-64). A variety of linkers and linkage chemistries are taught (see columns 25-32). The reference teaches that the linkage of two antibiotic moieties can create compounds of new activity (see column 1, lines 1-30) and that "two antibiotic moieties can be linked in which one is known to attack Gram positive bacteria and another to attack Gram negative bacteria" (see column 1, lines 27-30). Truett teaches a dimeric compound where one of the antibiotic moieties is ceftazidime (see column 3, line 7). Ceftazidime is a beta lactam antibiotic that reads on the elected species that is set forth in claim 53, see structure in the instant Figure 6B-2. Truett lacks the teaching of linking vancomycin with ceftazidime.

However, it was well known in the art at the time of filing to use combination therapy with vancomycin and ceftazidime. For example, Boeckh et al teach that this combination therapy is used to “cover a broad spectrum of gram positive and gram negative bacteria” (see page 92, 1st paragraph). The reference teaches the pharmacokinetics of the combination of vancomycin and ceftazidime, administered to humans (see Abstract and Table 1), thus pharmaceutical compositions of the drugs are well known.

Renoud-Grappin et al teach that one way to achieve effective combination therapy is to covalently link two different drugs. See page 208, first column, first full paragraph of the reference, which describes using heterodimers for combination therapy linked “through an appropriate spacer, in an attempt to combine the inhibitory capacity” of two different classes of molecules. The reference also describes that one would attempt such an approach to span two binding sites on the target. Renoud-Grappin et al also discuss combining different drugs to “prevent the emergence of drug-resistant virus strains” and set forth three main reasons for combination therapy (see page 207, 2nd column, 2nd paragraph). It is recognized that the linked compounds of Renoud-Grappin et al (see, for example, Figure 4 of the reference) are anti-virals and not antibiotics; however, it is the examiner’s position that one of ordinary skill would recognize the relevance of preventing the emergence of drug-resistant strains for both classes of molecules since such was well established in the art.

Additionally, vancomycin dimers were also known in the art at the time of filing. Staroske et al discuss both “head-to-head” and head-to-tail” dimers (see Figure 3) and that in “light of recent reports of vancomycin -resistant bacteria” there is a “strong incentive for the development of more potent antibiotics” (page 4917, bottom). The reference also teaches that dimeric vancomycin compounds exhibit improved antibacterial activity, see for example, page 4918, top. Specifically, the dimers of Staroske et al are linked from the amino terminus of one vancomycin moiety to the carboxy terminus of another (see Scheme 1, page 4919). The reference also contemplates linking of the vancomycin at the vancosamine moiety (see page 4920, last two paragraphs).

Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to link vancomycin and ceftazidime, based on the teaching of Truett concerning the linking of diverse antibiotic moieties combined with the teaching of Boeckh et al to perform combination therapy using the drugs, the teaching of Renoud-Grappin concerning linking drugs to perform combination therapy and the teaching of Staroske et al concerning vancomycin dimers linked through the amino and carboxy terminus. Specifically, Truett teaches that two antibiotics, one known to attack Gram positive bacteria and another to attack Gram negative bacteria can be linked and the advantages of doing such, and Boeckh et al teach that vancomycin and ceftazidime fulfill these requirements. Renoud-Grappin teach that one way to achieve effective combination therapy is to covalently link two different drugs. Finally, Staroske et

al teach that vancomycin can be linked at specific linkage sites. One of ordinary skill would have been motivated to covalently link vancomycin with ceftazidime to create a broad spectrum antibiotic compound to fight antibiotic resistant strains. One of ordinary skill would also have had a reasonable expectation of success based on the fact that Staroske et al teaches linking chemistry for vancomycin.

Response to Arguments

13. Applicant's arguments filed October 9, 2001 have been fully considered but are moot in view of the new grounds of rejection set forth in this action.

Status of Claims/Conclusion


14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maurie E. Garcia, Ph.D. whose telephone number is (703) 308-0065. The examiner can normally be reached on Monday-Thursday from 8:30 to 6:00 and alternate Fridays.

16. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jyothsna Venkat, can be reached on (703) 308-2439. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Maurie E. Garcia, Ph.D.
December 14, 2001


DR. JYOTHSNA VENKAT PH.D.
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